

09/444, 284

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Term:	knob and L4	
Display:	20	Documents in Display Format: -
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side by side			
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<u>L5</u>	knob and L4	5	<u>L5</u>
<u>L4</u>	l2 and L3	5	<u>L4</u>
<u>L3</u>	adenovir\$ near3 (12 or 16 or 28 or 40)	1361	<u>L3</u>
<u>L2</u>	liver with l1	7	<u>L2</u>
<u>L1</u>	(reduc\$ or decreas\$ or alter\$ or modif\$) near6 tropism near5 adenovir\$	152	<u>L1</u>

END OF SEARCH HISTORY

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- ☒ 1. [20040142473](#). 20 Feb 04. 22 Jul 04. Means and methods for fibroblast-like or macrophage-like cell transduction. Vogels, Ronald, et al. 435/456; C12N015/861.
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- ☐ 2. [20040043489](#). 22 Aug 03. 04 Mar 04. Gene delivery vectors provided with a tissue tropism for dendritic cells and methods of use. Havenga, Menzo, et al. 435/456; C12N015/861.
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- ☐ 3. [20040033605](#). 20 Mar 03. 19 Feb 04. Gene delivery vectors provided with a tissue tropism for dendritic cells. Havenga, Menzo, et al. 435/456; 435/372 C12N015/861 C12N005/08.
-
- ☐ 4. [20040002060](#). 24 Jan 03. 01 Jan 04. Fiber shaft modifications for efficient targeting. Kaleko, Michael, et al. 435/5; 435/235.1 435/320.1 435/325 435/456 435/69.3 530/350 536/23.72 C12Q001/70 C07H021/04 C12N007/00 C12N015/861 C07H021/02 C07K014/005.
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- ☐ 5. [20030215948](#). 27 Mar 03. 20 Nov 03. Fiber shaft modifications for efficient targeting. Kaleko, Michael, et al. 435/456; 435/235.1 435/320.1 435/370 C12N015/861 C12N007/00 C12N005/08.
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Terms	Documents
knob and L4	5

[Prev Page](#)[Next Page](#)[Go to Doc#](#)

09/444, 284

=> d his

(FILE 'HOME' ENTERED AT 18:29:32 ON 23 AUG 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:29:43 ON 23 AUG 2004

L1 208 S (REDUC? OR DECREAS? OR ALTER? OR MODIF?) (6A) TROPISM(5A) ADENOV
L2 37 S LIVER AND L1
L3 6079 S ADENOVIR?(3A) (12 OR 16 OR 28 OR 40)
L4 6 S L2 AND L3
L5 4 S KNOB AND L4
L6 1 DUP REM L5 (3 DUPLICATES REMOVED)
L7 3 DUP REM L4 (3 DUPLICATES REMOVED)

=> d bib ab l6

L6 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
AN 2003042985 MEDLINE
DN PubMed ID: 12551989
TI **Reduction of natural adenovirus tropism to the liver** by both ablation of fiber-coxsackievirus and adenovirus receptor interaction and use of replaceable short fiber.
AU Nakamura Takafumi; Sato Kenzo; Hamada Hirofumi
CS Department of Molecular Medicine, Sapporo Medical University, S1 W17, Chuo-ku, Sapporo 060-8556, Japan.. Nakamura.Takafumi@mayo.edu
SO Journal of virology, (2003 Feb) 77 (4) 2512-21.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20030129
Last Updated on STN: 20030316
Entered Medline: 20030314
AB The initial recognition and binding of adenovirus vector to the host cell surface is mediated by interaction between the adenovirus fiber **knob** protein and its receptor, the coxsackievirus and adenovirus receptor (CAR). This natural tropism of adenovirus vector needs to be ablated in order to achieve targeted gene transfer. To this end, we noted that **adenovirus** serotype 40 (Ad40) contains two distinct long and short fibers; the short fiber is unable to recognize CAR, while the long fiber binds CAR. We generated adenovirus serotype 5-based mutants with chimeric Ad40-derived fibers, which were composed of either long or short shafts together with CAR binding or nonbinding **knobs**. The capacity of these adenovirus mutants for in vitro and in vivo gene transfer to **liver** cells was examined. In the case of primary human hepatocytes displaying a high expression level of CAR and alphav integrin, both CAR binding ability and fiber shaft length played important roles in efficient transduction. Most significantly, the high transduction efficiency observed in the **liver** and spleen following intravenous administration of adenovirus vector was dramatically reduced by both ablation of fiber-CAR interaction and the use of replaceable short fiber. In other tissues displaying a low level of transduction, no significant differences in transduction efficiency were observed among adenovirus vector mutants. Furthermore, incorporation of a 7-lysine-residue motif at the C-terminal end of CAR-nonbinding short fiber efficiently achieved transduction of target cells via the heparan-containing receptor. Our results demonstrated that the natural tropism of adenovirus in vivo is influenced not only by fiber-CAR interaction but also by fiber shaft length. Furthermore, our strategy may be useful for retargeting adenovirus to particular tumors and tissue types with specific receptors.

=> d au ti so pi ab 1-3 17

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
IN Havenga Menzo, Jans Emco; Bout, Abraham; Vogels, Ronald
TI Adenoviral gene delivery vectors with cell type specificity for
mesenchymal stem cells and therapeutic uses

SO PCT Int. Appl., 63 pp.

CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004661	A2	20030116	WO 2002-NL443	20020705
WO 2003004661	A3	20031030		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1279738	A1	20030129	EP 2001-202619	20010706
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
EP 1406666	A2	20040414	EP 2002-746193	20020705
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			

AB The present invention provides novel methods and means for delivering a heterologous nucleic acid of interest to mesenchymal stem cells by providing recombinant adenoviral vectors provided with, or having a natural tropism for mesenchymal stem cells, typically in combination with a reduced tropism for other kinds of cells, in particular **liver** cells. The invention also provides mesenchymal stem cells provided with a heterologous nucleic acid through the use of a recombinant adenoviral vector according to the invention, and the use of such mesenchymal stem cells for the preparation of medicaments for the treatment of multiple sclerosis, rheumatoid arthritis, angiogenesis and bone related disorders, for instance in treatments that involve bone (re)generation.

L7 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1

AU Nakamura Takafumi; Sato Kenzo; Hamada Hirofumi

TI **Reduction** of natural **adenovirus tropism** to the **liver** by both ablation of fiber-coxsackievirus and adenovirus receptor interaction and use of replaceable short fiber.

SO Journal of virology, (2003 Feb) 77 (4) 2512-21.

Journal code: 0113724. ISSN: 0022-538X.

AB The initial recognition and binding of adenovirus vector to the host cell surface is mediated by interaction between the adenovirus fiber knob protein and its receptor, the coxsackievirus and adenovirus receptor (CAR). This natural tropism of adenovirus vector needs to be ablated in order to achieve targeted gene transfer. To this end, we noted that **adenovirus** serotype 40 (Ad40) contains two distinct long and short fibers; the short fiber is unable to recognize CAR, while the long fiber binds CAR. We generated adenovirus serotype 5-based mutants with chimeric Ad40-derived fibers, which were composed of either long or short shafts together with CAR binding or nonbinding knobs. The capacity of these adenovirus mutants for in vitro and in vivo gene transfer to **liver** cells was examined. In the case of primary human hepatocytes displaying a high expression level of CAR and alphav integrin, both CAR binding ability and fiber shaft length played important roles in

efficient transduction. Most significantly, the high transduction efficiency observed in the **liver** and spleen following intravenous administration of adenovirus vector was dramatically reduced by both ablation of fiber-CAR interaction and the use of replaceable short fiber. In other tissues displaying a low level of transduction, no significant differences in transduction efficiency were observed among adenovirus vector mutants. Furthermore, incorporation of a 7-lysine-residue motif at the C-terminal end of CAR-nonbinding short fiber efficiently achieved transduction of target cells via the heparan-containing receptor. Our results demonstrated that the natural tropism of adenovirus in vivo is influenced not only by fiber-CAR interaction but also by fiber shaft length. Furthermore, our strategy may be useful for retargeting adenovirus to particular tumors and tissue types with specific receptors.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 IN Vogels, Ronald; Schouten, Govert Johan; Bout, Abraham
 TI Adenoviral vectors with low antigenicity for delivery of nucleic acids to
 synoviocytes for the gene therapy of rheumatoid arthritis
 SO PCT Int. Appl., 131 pp.
 CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052186	A1	20000908	WO 2000-NL133	20000303
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1159438	A1	20011205	EP 2000-908116	20000303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537816	T2	20021112	JP 2000-602796	20000303
NZ 527290	A	20040326	NZ 2000-527290	20000303
NZ 527634	A	20040326	NZ 2000-527634	20000303
NZ 527635	A	20040326	NZ 2000-527635	20000303

AB The invention provides a nucleic acid delivery vehicle with or having been provided with at least a tissue tropism for fibroblast-like or macrophage-like cells, preferably synoviocytes. In one aspect said nucleic acid delivery vehicle is a virus capsid or a functional part, derivative and/or analog thereof. Preferably said virus capsid is an adenovirus capsid. Preferably said adenovirus is a subgroup B **adenovirus**, preferably **adenovirus 16**. Preferably said tissue tropism is provided by at least a tissue tropism determining part of an adenovirus fiber protein or a functional derivative and/or analog thereof. The invention further presents methods for the treatment of diseases, preferably joint related diseases.

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